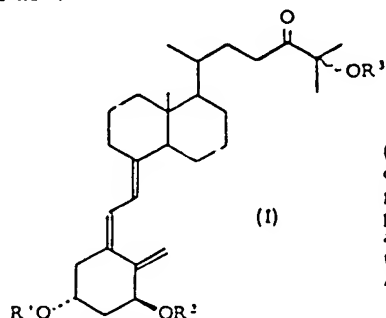


50771 D/28 B05 (B01) TEIJ 26.10.79  
TEIJIN KK \*J56061-351  
26.10.79-JP-137771 (26.05.81) A61k-31/59 C07c-172  
1-Alpha, 25-dihydroxy-24-oxo:cholecalciferol deriva-  
exhibit vitamin/D 3 pharmacological activities. prepd. from  
24-oxo-cholesta-5,7-diene cpds.

1a, 25-Dihydroxy-24-oxocholecalciferols of formula (I)  
are new:



(R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> = H  
or hydroxy protecting  
gp. (pref. 1-12C ali-  
phatic or aromatic  
acyl, trialkylsilyl, 2-  
tetrahydropyranyl, or  
2-tetrahydrofuranyl)).

B(1-D2, 3-G). 2

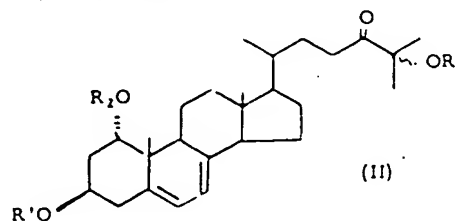
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#### USE/ADVANTAGE

(I) exhibit vitamin D<sub>3</sub>-like pharmacological activities.  
On reduction of the 24-oxo, (I) are converted into 1a, 24,  
25-trihydroxyvitamin D<sub>3</sub> as active vitamin D<sub>3</sub>.

#### PREPARATION

(I) are prepd. by irradiating 1a, 25-dihydroxy-24-oxo-  
cholesta-5,7-dienes (II) with ultraviolet rays to yield 1a, 25-  
dihydroxy-24-oxoprevitamins D<sub>3</sub>, isomerising the latter  
with thermal energy, if required followed by removal of the  
hydroxy protecting gp.



J56061351+

The UV rays pref. have wavelength 200-360 nm, esp. 260-  
310 nm. The reaction is conducted in an inert solvent-  
including hydrocarbons and haloalkohydrocarbons (e.g. hexane,  
heptane, PhH, PhMe, xylene, PhCl), ethers (e.g. Et<sub>2</sub>O, THF,  
dioxane), and alcohols (e.g. MeOH, EtOH, PrOH) at a temp.  
of -20°C to 120°C, pref. -10°C to 50°C. The subsequent  
thermal isomerisation is carried out at 20-120°C, pref.  
40-100°C in the inert solvent.

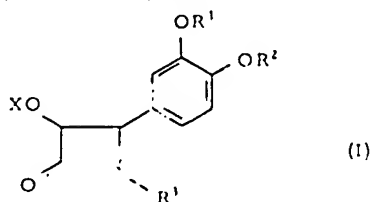
#### EXAMPLE

A soln. of 70 mg 1a, 3β, 25-trihydroxy-24-oxocholesta-5,7-  
diene dissolved in a mixt. of 50 mg deoxygenated EtOH and  
500 ml Et<sub>2</sub>O was irradiated with a 200W lamp surrounded by  
a Vycor filter at 10-20°C with stirring for 6 hrs. The  
cold soln. was evapd. in vacuo at 30°C, and the residue was  
dissolved in 250 ml deoxygenated PhH and refluxed under  
heating for 2.5 hr. After the reaction completion, the mixt.  
was evapd. in vacuo, and the resulting residue was chroma-  
tographed on a thin layer of silica gel preliminarily treat-  
ed with 2% AgNO<sub>3</sub>-MeCN (solvent:CHCl<sub>3</sub>-MeOH) and of sil-  
ica gel (PhH-Me<sub>2</sub>CO) to give 10.8 mg 1a, 25-dihydroxy-24-  
oxovitamin D<sub>3</sub>, mp. 91-93.5°C. (6ppW52)

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50772 D/28 B03 SAGA 24.10.79  
SAGAMI CHEM RES CENTRE \*J56061-352  
24.10.79-JP-134485 (26.05.81) C07c-101/77 C07d-205/08  
3-Hydroxy-beta-lactam cpds. can be prepd. economically -  
and are used in DOPA prepn. used in antiparkinson  
treatment.

3-Hydroxy-β-lactam cpds. of formula (I) are new:



(R<sup>1</sup> and R<sup>2</sup> = H, lower alkyl, benzyl or acyl, or R<sup>1</sup> and R<sup>2</sup>  
taken together may form alkylene;  
R<sup>3</sup> = alkyl, aryl or heteroaromatic gp.;  
X = H, benzyl or tosyl).

#### USE/ADVANTAGE

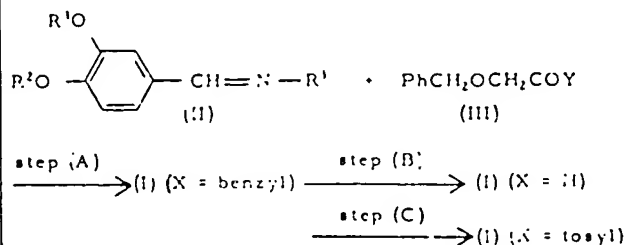
(I) can be converted into DOPA (useful as antiparkinson-

B(6-A2, 7-D1). 2

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ism agent) on reaction with NaN<sub>3</sub>, cleavage of the β-lactam  
ring, and acid treatment. (I) can be prepd. from cheap  
raw material.

#### PREPARATION



(Y is not defined but probably halogen).

Step (A) is carried out in a solvent, e.g. PhH, PhMe, THF,  
CH<sub>2</sub>Cl<sub>2</sub>, in presence of a tert. amine, e.g. Et<sub>3</sub>N, Pr<sub>3</sub>N,  
Bu<sub>3</sub>N, pyridine, N-methylpiperidine, N-methylpyrrolidine  
DBU, at -78°C to 100°C.

J56061352+

Step (B) comprises hydrogenolysis with Pd catalyst (e.g. Pd black, Pd-C) in a solvent (e.g. MeOH, EtOH, CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, PhH, PhMe, THF, MeCN, DMF) at room temp. to 150°C, pref. 50-100°C.

Step (C) comprises tosylation with p-TsCl in presence of a tert-amine in an aprotic solvent (e.g. CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, PhH, PhMe, THF, MeCN, Me<sub>2</sub>CO, DMF, DMSO) at -30°C to 100°C.

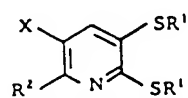
#### EXAMPLE

To a soln. of 5.00 g 3,4-dimethoxybenzylideneaniline and 2.50 g Et<sub>3</sub>N in 50 ml PhH was dropwise added slowly a soln. of 4.60 g benzyloxyacetyl chloride in 50 ml PhH under ice cooling. The reaction mixt. was gradually warmed up to room temp., stirred for 15 hrs., washed with water, dried on MgSO<sub>4</sub>, and evapd. in vacuo to give 8.18 g light yellow oil. This was chromatographed on silica gel and eluted with n-hexane-EtOAc (4:1) to give 4.16 g cis-isomer of 1-phenyl-3-benzyloxy-4-(3,4-dimethoxyphenyl)azetidin-2-one as white crystals, m. pt. 130-133°C, and 2.38 g trans-isomer as a colourless oil, n<sub>D</sub><sup>20</sup>: 1.6018, (10ppW52).

J56061352

50774 D/28 B03 C02 E13 M:ITU 23.10.79  
MITSUBISHI CHEM IND KK \*J56061-354  
23.10.79-JP-136740 (26.05.81) C07d:211/90 C07d:213/80  
Nicotinic acid derivs. - used as agrochemicals, drugs and chemical intermediates

Nicotinic acid derivs. of formula (I) are new:



(I)

(R¹ = lower alkyl (e.g. Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu);  
R² = H, lower alkyl or aryl (e.g. phenyl, tolyl);

X = lower alkoxy-carbonyl (e.g. MeOCO-, EtOCO-, n-PrOCO-, i-PrOCO-) or COOH).

#### USE

(I) are utilized as agrochemicals or drugs or as raw material in production of various chemicals. (I) can be converted into nicotinic acid or its esters by removal of -SR¹ on hydrogenolysis with Raney Ni catalyst.

#### PREPARATION

the solvent used, pref. room temp. to 100°C, for a period of 0.1-10 hrs., pref. 0.5-5 hrs.

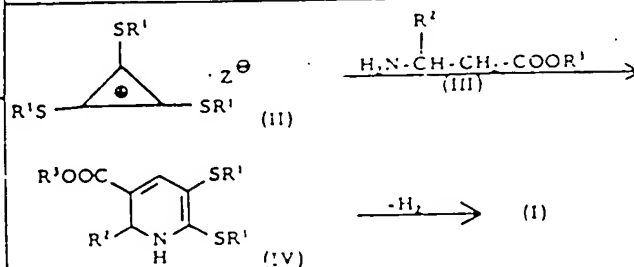
The subsequent dehydration is achieved by allowing (IV) to stand in a halogenohydrocarbon solvent, e.g. CHCl<sub>3</sub>, CCl<sub>4</sub>, fluorohydrocarbon, perfluorohydrocarbon, at 0°C to the reflux temp. of the solvent used, pref. room temp., for a period of 3-24 hrs., pref. 10-15 hrs.

#### EXAMPLE

A mixt. of tri-t-butylthiocyclopropenium perchlorate (1 mmole, 403 mg.) and methyl α-aminopropionate (2 mmole) in 40 ml. DMF is allowed to stand at 80°C in presence of NaH (3 mmole) for 1 hr. Water is added, and the mixt. is extracted with hexane. The extract is dried on Na<sub>2</sub>SO<sub>4</sub> and evapd., the residue is chromatographed on silica gel to give methyl 2,3-di-t-butylthio-1,6-dihydronicotinate in 72% yield.

This is dissolved in 10 ml. CCl<sub>4</sub> and allowed to stand under air for 2 hrs. to give methyl 2,3-di-t-butylthio-nicotinate in quantitative yield. (5ppW52)

BC(7-D4) E(7-D4) N(5-A). 1



(Z⁻ = anion (e.g. halogen ion, ClO<sub>4</sub>⁻, BF<sub>4</sub>⁻, SbF<sub>6</sub>⁻, SbCl<sub>6</sub>⁻, AlCl<sub>4</sub>⁻);  
R¹ = lower alkyl).

#### DETAILS

(II) has been described in J48096564.

The reaction is carried out in a solvent, e.g. CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, dimethoxyethane, DMF, MeOH, pref. in presence of a base, e.g. NaH, t-BuOK, at -100°C to the reflux temp. of

J56061354

J56061354